

Cochrane Database of Systematic Reviews

Probiotics for people with hepatic encephalopathy (Review)

Dalal R, McGee RG, Riordan SM, Webster A	٩C
--	----

Dalal R, McGee RG, Riordan SM, Webster AC. Probiotics for people with hepatic encephalopathy. *Cochrane Database of Systematic Reviews* 2017, Issue 2. Art. No.: CD008716. DOI: 10.1002/14651858.CD008716.pub3.

www.cochranelibrary.com



[Intervention Review]

Probiotics for people with hepatic encephalopathy

Rohan Dalal¹, Richard G McGee², Stephen M Riordan³, Angela C Webster⁴

¹Sydney Medical School, Westmead Hospital, Sydney, Australia. ²Institute of Endocrinology and Diabetes, The Children's Hospital at Westmead, Westmead, Australia. ³Gastrointestinal and Liver Unit, The Prince of Wales, Randwick, Australia. ⁴Sydney School of Public Health, The University of Sydney, Sydney, Australia

Contact address: Richard G McGee, dr.richardmcgee@gmail.com.

Editorial group: Cochrane Hepato-Biliary Group.

Publication status and date: Edited (no change to conclusions), published in Issue 1, 2021.

Citation: Dalal R, McGee RG, Riordan SM, Webster AC. Probiotics for people with hepatic encephalopathy. *Cochrane Database of Systematic Reviews* 2017, Issue 2. Art. No.: CD008716. DOI: 10.1002/14651858.CD008716.pub3.

Copyright © 2017 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Background

Hepatic encephalopathy is a disorder of brain function as a result of liver failure or portosystemic shunt or both. Both hepatic encephalopathy (clinically overt) and minimal hepatic encephalopathy (not clinically overt) significantly impair patient's quality of life and daily functioning, and represent a significant burden on healthcare resources. Probiotics are live micro-organisms, which when administered in adequate amounts, may confer a health benefit on the host.

Objectives

To determine the beneficial and harmful effects of probiotics in any dosage, compared with placebo or no intervention, or with any other treatment for people with any grade of acute or chronic hepatic encephalopathy. This review did not consider the primary prophylaxis of hepatic encephalopathy.

Search methods

We searched The Cochrane Hepato-Biliary Group Controlled Trials Register, CENTRAL, MEDLINE, Embase, Science Citation Index Expanded, conference proceedings, reference lists of included trials, and the World Health Organization International Clinical Trials Registry Platform until June 2016.

Selection criteria

We included randomised clinical trials that compared probiotics in any dosage with placebo or no intervention, or with any other treatment in people with hepatic encephalopathy.

Data collection and analysis

We used standard methodological procedures expected by The Cochrane Collaboration. We conducted random-effects model metaanalysis due to obvious heterogeneity of participants and interventions. We defined a P value of 0.05 or less as significant. We expressed dichotomous outcomes as risk ratio (RR) and continuous outcomes as mean difference (MD) with 95% confidence intervals (CI).

Main results

We included 21 trials with 1420 participants, of these, 14 were new trials. Fourteen trials compared a probiotic with placebo or no treatment, and seven trials compared a probiotic with lactulose. The trials used a variety of probiotics; the most commonly used group of probiotic was VSL#3, a proprietary name for a group of eight probiotics. Duration of administration ranged from 10 days to 180 days. Eight trials declared their funding source, of which six were independently funded and two were industry funded. The remaining 13 trials did not disclose their funding source. We classified 19 of the 21 trials at high risk of bias.



We found no effect on all-cause mortality when probiotics were compared with placebo or no treatment (7 trials; 404 participants; RR 0.58, 95% CI 0.23 to 1.44; low-quality evidence). No-recovery (as measured by incomplete resolution of symptoms) was lower for participants treated with probiotic (10 trials; 574 participants; RR 0.67, 95% CI 0.56 to 0.79; moderate-quality evidence). Adverse events were lower for participants treated with probiotic than with no intervention when considering the development of overt hepatic encephalopathy (10 trials; 585 participants; RR 0.29, 95% CI 0.16 to 0.51; low-quality evidence), but effects on hospitalisation and change of/or withdrawal from treatment were uncertain (hospitalisation: 3 trials, 163 participants; RR 0.67, 95% CI 0.11 to 4.00; very low-quality evidence; change of/or withdrawal from treatment: 9 trials, 551 participants; RR 0.70, 95% CI 0.46 to 1.07; very low-quality evidence). Probiotics may slightly improve quality of life compared with no intervention (3 trials; 115 participants; results not meta-analysed; low-quality evidence). Plasma ammonia concentration was lower for participants treated with probiotic (10 trials; 705 participants; MD -8.29 μ mol/L, 95% CI -13.17 to -3.41; low-quality evidence). There were no reports of septicaemia attributable to probiotic in any trial.

When probiotics were compared with lactulose, the effects on all-cause mortality were uncertain (2 trials; 200 participants; RR 5.00, 95% CI 0.25 to 102.00; very low-quality evidence); lack of recovery (7 trials; 430 participants; RR 1.01, 95% CI 0.85 to 1.21; very low-quality evidence); adverse events considering the development of overt hepatic encephalopathy (6 trials; 420 participants; RR 1.17, 95% CI 0.63 to 2.17; very low-quality evidence); hospitalisation (1 trial; 80 participants; RR 0.33, 95% CI 0.04 to 3.07; very low-quality evidence); intolerance leading to discontinuation (3 trials; 220 participants; RR 0.35, 95% CI 0.08 to 1.43; very low-quality evidence); change of/or withdrawal from treatment (7 trials; 490 participants; RR 1.27, 95% CI 0.88 to 1.82; very low-quality evidence); quality of life (results not meta-analysed; 1 trial; 69 participants); and plasma ammonia concentration overall (6 trials; 325 participants; MD -2.93 μ mol/L, 95% CI -9.36 to 3.50; very low-quality evidence). There were no reports of septicaemia attributable to probiotic in any trial.

Authors' conclusions

The majority of included trials suffered from a high risk of systematic error ('bias') and a high risk of random error ('play of chance'). Accordingly, we consider the evidence to be of low quality. Compared with placebo or no intervention, probiotics probably improve recovery and may lead to improvements in the development of overt hepatic encephalopathy, quality of life, and plasma ammonia concentrations, but probiotics may lead to little or no difference in mortality. Whether probiotics are better than lactulose for hepatic encephalopathy is uncertain because the quality of the available evidence is very low. High-quality randomised clinical trials with standardised outcome collection and data reporting are needed to further clarify the true efficacy of probiotics.

PLAIN LANGUAGE SUMMARY

Probiotics for people with hepatic encephalopathy

Why the review is important

Hepatic encephalopathy is a disorder of brain function as a result of liver failure or portosystemic shunt or both. Both hepatic encephalopathy (clinically overt) and minimal hepatic encephalopathy (not clinically overt) significantly impair patient's quality of life and daily functioning and represent a significant burden on healthcare resources. Probiotics are live micro-organisms, which when administered in adequate amounts may confer a health benefit on the host. We searched and summarised randomised trials about the benefits and harms of any probiotic in any dosage, compared with placebo or no intervention, or with any other treatment for people with any grade of acute or chronic hepatic encephalopathy.

Main findings

The evidence is current to June 2016. Of the 21 included trials including 1420 participants, 14 trials compared a probiotic with placebo or no treatment and seven trials compared a probiotic with lactulose. The treatment duration of the trials ranged from 10 days to 180 days.

Compared with placebo or no intervention, probiotics probably improve recovery and may lead to improvements in the development of overt hepatic encephalopathy, quality of life, and plasma ammonia concentrations, but may lead to little or no difference in mortality. Probiotics may slightly improve quality of life when compared with no intervention; however, this conclusion is based on three trials with low-quality evidence. Whether probiotics are better than lactulose for hepatic encephalopathy is uncertain because the quality of the available evidence was very low. There were no reports of septicaemia attributable to probiotic in any trial. There was no evidence of more adverse events with probiotics when compared to placebo or lactulose.

Funding

Eight trials declared their funding source, of which six were independently funded and two were industry funded. The remaining 13 trials did not disclose their funding source.

Limitations of the review

Many of the included trials suffered from a high risk of systematic error ('bias') and a high risk of random error ('play of chance'). Accordingly, we consider the evidence to be of low quality.

Conclusions

Compared with placebo or no intervention, probiotics probably improve recovery and may lead to improvements in the development of overt hepatic encephalopathy, quality of life, and plasma ammonia concentrations, but probiotics may lead to little or no difference in mortality. Whether probiotics are better than lactulose for hepatic encephalopathy is uncertain because the quality of the available



evidence was very low. High-quality randomised clinical trials with standardised outcome collection and data reporting are needed to further clarify the true efficacy of probiotics.